UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

MEMORANDUM

OFFICE OF THE
SCIENCE ADVISOR

FROM: Warren E. Lux, M.D.
EPA Human Subjects Research Review Official

TO: Robert Truckner, M.D., M.P.H.
Director, NHEERL Human Research Protocol Office

SUBJECT: Continuing Approval of Research Involving Human Subjects

DATE: September 8, 2008

The study cited below represents a major modification of a prior HSRRO-approved study that was previously entitled *Mechanisms by Which Ozone Exacerbates Asthma in Adults with Mild Asthma* (husulg# 06-40). I re-reviewed the study at your request because the extent of the modification was so great as to require re-review in your judgment. On the basis of the re-review, I concluded that the modified study as set forth in the current protocol continues to qualify as research involving human subjects that complies with EPA Regulation 40 CFR 26 (**Protection of Human Subjects**). The finding of continued compliance includes the determination that the research remains non-exempt under 40 CFR 26.101(b), that it has been approved by the IRB of record, and that the institution engaged in the research has a valid Federalwide Assurance on file with the HHS Office for Human Research Protections. Accordingly, the prior HSRRO approval for recruitment and enrollment of human research subjects remains in effect.

Study Title:	*Mechanisms by Which Air Pollution Particles Exacerbate Asthma in Older Adults with Mild Asthma*
Engaged Institution:	National Health and Environmental Effects Research Laboratory, U.S. EPA
FWA #:	FWA00012755
Principal Investigator:	Martha Sue Carraway, M.D.
EPA HSRR #:	I08-0037P

CC: Martha Sue Carraway

Dr. R. Julian Preston, PhD
Acting Associate Director for Health
USEPA
MD B105-01
RTP, NC 27711

Date Aug 19, 2008

IRB Study # 06-0548

Title of Study: Mechanisms by which air pollution particles exacerbate asthma in older adults with mild asthma.

We are requesting a review of major revisions of the above study. These modifications have been approved by the UNC IRB. The major changes in this protocol are:

1) We have changed the exposure substance from ozone to concentrated fine and ultrafine air pollution particles.
2) We have eliminated sputum induction. To obtain samples from the lower respiratory tract, we will perform bronchoscopy on the day following exposure.
3) We have eliminated measurement of exhaled nitric oxide as an end point.
4) We will not require subjects to exercise during the exposure.
5) We have added a screening session for genotyping that will occur prior to the training day. At this visit, subjects will be screened briefly by the nursing staff for confounding medical issues that would exclude the subject from the study. A new consent form and the nursing questionnaire for the screening visit have been added, and both documents are attached. This will potentially eliminate unnecessary subject visits for the training day if they do not qualify by genotype after we have accumulated sufficient subjects in one genotype arm.
6) All subjects will receive both air and air pollution exposure; each exposure will be followed by bronchoscopy, so that each subject will undergo two bronchoscopies. The previous protocol had a provision for only exposing the remaining subjects to ozone after the first ten subjects had been exposed, if there were no significant differences in pulmonary function after the ozone exposure. Given the relatively small number of subjects, it is scientifically preferred to use each subject as their own control, thus having each subject also do an air exposure.

This packet contains the following documents:

Cover memo
NHEERL sign-off sheet with signatures
NHEERL Fact Sheet
NHEERL Study Justification Document
IRB approval letter
Research protocol as approved by the IRB
Consent forms approved and stamped by the IRB
Questionnaires and advertising approved and stamped by the IRB
Ethics training reports required by the IRB

Thank you for your consideration, if you have further questions, pleas let me know.

Sincerely,

Martha Sue Carraway, MD
Human Studies Division
US Environmental Protection Agency
MD 58D
RTP, NC 27711

NHEERL HUMAN RESEARCH SIGN-OFF SHEET

PI *(Name/Division)*: Carraway, Martha S

PROTOCOL TITLE: Mechanisms by which air pollution particles exacerbate asthma in older adults with mild asthma.

NAME OF APPROVING IRB: University of North Carolina

IRB-ASSIGNED PROTOCOL NUMBER: 06-0548

REVIEWS *(Attach to EPA Protocol Package)*		
Reviewer	**Name**	**Date**
Peer Reviewer1 *(printed or typed)*		
Peer Reviewer2 *(printed or typed)*		
Statistician		
Physician		
Other		
APPROVALS		
Official	**Signature**	**Date**
Branch Chief		
Division Human Research Officer		
IRB	*(Attach signed approval letter)*	
Dosing Review Officer		
Division Quality Assurance Officer		
Division Director		
HRPO Director		
Associate Director for Health or Ecology	*(Indicated by approval letter)*	
Agency Human Subjects Research Review Official	*(Indicated by approval letter)*	